

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

In the specification, paragraphs have been amended on page 1 and on page 24.

Claims 11 – 17, 28, 29, 37 and 44 are cancelled.

Claims 1, 6, 18, 26, 32, 33, 34 – 36, 40 – 43, 47 – 49, 52, 57 and 59 – 63 are currently amended.

Claims 53 – 56 are withdrawn from consideration.

Claims 66 and 67 were added.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 1 – 10, 18 – 27, 30 – 36, 38 – 43, 45 – 52 and 57 – 66 are now pending in this application.

I. Allowable Subject Matter

Applicants acknowledge the Examiner's statements on page 12 of the Office Action regarding the allowability of claims 33 – 37, 40 – 46, 48 – 52 and 57 – 62. The Examiner states that these claims "contain limitations allowable over the prior art of record with does not teach mAb 679 and does not teach the conjugates recited in claims 48, 52, 57 and 61 – 62."

II. Election/Restriction

Applicants acknowledge the fact that the Examiner expanded his search to include Groups I and II. Applicants further acknowledge that the Examiner has withdrawn claims 53 – 56 from consideration in the present application.

III. Objections to the Specification

Applicants have amended the cross-reference to related applications and have updated the status of applications to which reference is made in the specification, thus obviating the objections to the specification enunciated on page 2 of the Office Action. Withdrawal of the objections is respectfully requested.

IV. Objection to Claim 17

The Examiner has objected to claim 17 due to the fact that the Fluorine isotope is incorrectly recited. This rejection has been rendered moot in light of the cancellation of claim 17. Withdrawal of the objection is respectfully requested.

V. Rejection of Claims 4 – 8 as Allegedly Substantial Duplicates of Claims 12, 15, 17, 28 and 29

On page 3 of the Office Action, the Examiner has rejected claims 4 – 8 as alleged substantial duplicates of claims 12, 15, 17, 28 and 29. While not acquiescing to the Examiner's position, and simply in an effort to expedite the prosecution of this application, Applicants have cancelled claims 12, 15, 17, 28 and 29, thus rendering the Examiner's rejection moot. Reconsideration and withdrawal of this rejection is respectfully requested.

VI. Rejection of Claims 33 – 36 and 40 – 46 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 33 – 36 and 40 – 46 as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner alleges that it is not clear whether the monoclonal antibodies recited in these claims are publicly available.

The Examiner suggests that Applicants may overcome this rejection by showing, *inter alia*, that “[t]he complete V-region sequence of both H and L chains was known,” or “[t]he monoclonal antibody is recited in a claim of an issued U.S. Patent.”

Applicants assert that Mu-9 and MN-14 are both publicly available. Applicants direct the Examiner’s attention to the publication of Krishan *et al.*, where the V-region sequences for Mu-9 antibody (a.k.a., colon-specific antigen-p) has been elucidated (Krishnan *et al.*, *Cancer (suppl.)* 80:2667-2674, (1997)). See also U.S. Patent No. 6,096,289 (Goldenberg). Further, MN-14 is recited in claim 11 of U.S. Patent No. 5,981,504 (Buchsbaum).

Applicants also assert that mAb 679 is sufficiently described for the purposes of 35 U.S.C. § 112, first paragraph because Applicants disclose the complete V-region sequence of both the H and L chains in Figures 1 and 2.

Applicants assert that they have shown that either the antibodies recited in the above-mentioned claims were publicly available and/or that the antibodies are adequately described in the instant specification. Thus, Applicants believe that they have overcome the rejection under 35 U.S.C. § 112, first paragraph. Reconsideration and withdrawal of the rejection is respectfully requested.

VII. Rejection of Claims 1 – 52 and 57 – 65 Under 35 U.S.C. § 112, Second Paragraph

A. Claim 1 allegedly confusing vis-à-vis the recitation of “enzymes”

Applicants assert that claim 1 is not confusing vis-à-vis the recitation of enzymes. The specification discusses exemplary enzymes or enzyme classes contemplated by the invention on page 22, line 16 to page 24, line 10. The discussion in these pages of the specification describes how such enzymes would be employed, *inter alia*, to activate a prodrug at a target site. Some representative enzymes or enzyme classes discussed in these pages of the specification include carboxylesterases, carboxypeptidases, lactamases, glucuronidases and phosphatases. In short, the specification is very clear as to what is meant by an “enzyme” in the context of claim 1. Thus, claim 1 is not indefinite, as the Examiner alleges.

The Examiner has led Applicants to believe that the confusion about claim 1 is created by the fact that ribonuclease and DNAase I, both of which are recited as toxins in claim 12 (and also claim 5), are, according to the Examiner, also enzymes. Applicants assert that ribonuclease and DNase I are, in fact, considered toxins. *See Deonarain et al., Tumor Targeting 1:177 (1995)* (describing an antibody-toxin fusion protein having an RNase moiety); and *Linardou et al., Cell Biophys. 24-25:243 (1994)* (describing an antibody-toxin fusion protein comprising a DNase I component). In light of these citations, Applicants assert that claim 5 properly recites ribonuclease and DNase as toxins. Thus, the skilled artisan would not be “confused” by the recitation of ribonuclease and DNase as toxins. In short, claim 5 is definite vis-à-vis referring to ribonuclease and DNase as toxins. Reconsideration and withdrawal of this rejection is respectfully requested.

B. Claim 6 is not clear in reciting “further comprising a therapeutic nuclide”

Applicants assert that the rejection of claim 6 has been rendered moot in light of the amendments to claim 6. Reconsideration and withdrawal of the rejection is respectfully requested.

C. Claims 34 and 41 are unclear in light of the recitation of claims 33 and 40; Claims 36 and 37 are unclear in light of the recitation of claim 33; and Claims 43 and 44 are unclear in light of the recitation of claim 40

On page 5 of the Office Action, the Examiner has rejected claims 34 and 41 as allegedly being unclear “in relation to base claims 33 and 40, respectively.” Likewise, the Examiner has rejected claims 36 and 37 as allegedly being unclear in relation to base claim 33. Lastly, the Examiner has rejected claims 43 and 44 as allegedly being unclear in relation to base claim 40.

Applicants have amended claims 33, 34, 36, 40, 43 and 44 to more clearly claim what Applicants regard as their invention. Applicants believe that the amendments to the aforementioned claims, in addition to the cancellation of claim 37, also overcome the rejections of those claims on page 5 of the Office Action. Reconsideration and withdrawal of the rejection are respectfully requested.

D. Rejection of claims 48, 52, 55 and 61 – 63

On page 5 of the Office Action, the Examiner has rejected claims 48, 52, 55 and 61 - 63 as allegedly being unclear as to which moiety of the targetable conjugate that the “other arm” of the bispecific antibody binds to. Applicants believe that the rejection of the afore-mentioned claims is overcome by the amendments to claims 48, 52, 55 and 61 – 63. Reconsideration and withdrawal of the rejection is respectfully requested.

E. Rejection of claims 48, 52, 55 and 61 – 62

On page 6 of the Office Action, claims 48, 52, 55 and 61 – 62 have been rejected because “members (d) and (e)” are allegedly indefinite. The Examiner alleges that it is not clear what the “squiggly” bond between the “NH” and “D-Ala” represents.

Applicants assert that the so-called squiggly bond between the “NH” and “D-Ala” does not render the rejected claims indefinite. The “squiggly” bond is merely a simple chemical representation of the bond between the thiourea moiety of the conjugate and the rest of the peptide. The ordinary skilled artisan would understand that the “NH” to which the Examiner refers is the “NH” from the amino terminus of the D-Ala moiety. Thus, the “squiggly” bond does not render the rejected claims indefinite. Reconsideration and withdrawal of the rejection is respectfully requested.

F. Rejection of claims 59 and 60 for lack of antecedent basis

On page 6 of the Office Action the Examiner has rejected claims 59 and 60 as lacking antecedent basis for “said virus” and “said bacterium,” respectively. Applicants believe that the introduction of new claim 66 and the amendments to claims 59 and 60 overcome the rejection. Reconsideration and withdrawal of the rejection is respectfully requested.

G. Rejection of claims 61 – 63 as allegedly being unclear by reciting “intraoperatively,” “endoscopic,” and “intravascular”

On page 6 of the Office Action, the Examiner has rejected claims 61 – 63 as allegedly being unclear by reciting “intraoperatively,” “endoscopic,” and “intravascular” without a recitation of a step referring to an operation, to an endoscope or to an I.V. injection.

Applicants believe that the amendments to claims 61 – 63 render this rejection moot. Support for the amendments to claims 61 – 63 may be found in U.S. Patent No. 6,096,289, which is incorporated by reference into the instant specification. A copy of the '289 patent is submitted herewith for the Examiner's convenience. Reconsideration and withdrawal of the rejection is respectfully requested.

VIII. Rejection of Claims Under 35 U.S.C. § 102(b) and 103(a)

On pages 6 – 12, the Examiner has rejected many claims as being allegedly anticipated and/or rendered obvious by the disclosures of U.S. Patent No. 5,274,076 (Barbet), WO99/66951 (Hansen), U.S. Patent No. 4,818,709 (Primus), and U.S. Patent No. 6,096,289 (Goldenberg).

Applicants note that the Examiner, at page 12 of the Office Action, acknowledges that none of the above-mentioned references, alone or in combination, teach mAb 679.

Applicants assert, therefore, that the rejections under 35 U.S.C. § 102(b) and 103(a) have been overcome, since claim 1, as amended, now recites that the "other" arm of the bi-specific antibody or antibody fragment comprises the Fv of mAb 679. Reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b) and 103(a) is therefore respectfully requested.

IX. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

Examiner Saunders is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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